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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/329,917	06/10/99	CORDON-CARDO	C 55293-B/JPW/

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EXAMINER	
SOUAYA, J	
ART UNIT	**PAPER NUMBER**
1655	9

DATE MAILED: 07/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/329,917	Applicant(s) Cordon-Cardo
	Examiner Jehanne Souaya	Art Unit 1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 27, 2001*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *4,5*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 is broadly drawn to a method for determining the aggressiveness of a prostate carcinoma comprising detecting the presence of p27 protein in a sample of prostate carcinoma, the absence of p27 indicating that the prostate carcinoma is aggressive. Claims 2-3 are broadly drawn to a method of diagnosing benign prostate hyperplasia by obtaining a sample of the hyperplasia and detecting the presence of p27 protein or mRNA, wherein a decrease of p27 indicates that the hyperplasia is benign.

The specification teaches a study that measured whether loss of p27 expression was common in prostate cancer and teaches analyzing 74 prostate carcinomas from primary and metastatic sites (see p. 24). The specification teaches that 12 out of 42 of the primary prostatic carcinomas showed an intense nuclear immunoreactive p27 pattern while the remaining 30

showed altered patterns of expression. The specification teaches that out of the remaining 30 primary neoplasms, 12 had undetectable p27 levels, 18 had heterogenous pattern of expression. The specification teaches that out of 32 metastatic lesions, 21.9% showed intense p27 immunostaining, and 78.1% had heterogenous or undetectable nuclear expression of p27.

With regard to claim 1, from this data alone, it is unclear whether lack of p27 expression is indicative of aggressive prostate cancer as 12 out of 30 primary prostatic carcinomas showed undetectable p27, and 21.9% of metastatic lesions, showed intense levels of p27. It is further unclear from the teachings in the specification whether the primary neoplasms were isolated tumors that did not lead to metastasis (less aggressive than tumors that lead to metastasis). The specification teaches that disease aggressiveness was evaluated as the time to PSA failure (p 26). The unpredictability of lack of p27 expression and aggressiveness of prostate carcinoma is further exemplified by the specification which teaches that a trend toward an association was observed between a p27 negative phenotype and early relapse, however this difference was not statistically significant. Further unpredictability is found in the teachings of the specification that found that 12 cases of benign prostate hyperplasia, presumed to be unaggressive, showed low to undetectable p27 expression (p 26). Thus it cannot be determined from the teachings in the specification whether the aggressiveness of a prostate carcinoma can be determined based solely on the lack of expression of p27.

The art does not make up for the lack of guidance and the unpredictability taught in the specification. The art is further unpredictable regarding p27 levels and cancer as exemplified by

the teachings of Lloyd et al (American Journal of Pathology, vol. 154, 1999) that recent observations of increased p27 in several human breast cancer cell lines compared with normal mammary epithelial cells were surprising and difficult to explain (p 320). Lloyd further teaches that additional experiments done by transfecting normal and neoplastic mammary lines with vector containing p27 showed that the increased expression of p27 was associated with decreased cyclin D1 in the neoplastic MCF7 cell line but not in the normal cell line, and slightly increased levels of cyclin E protein in both cell lines indicated that the role of multiple interacting CDKIs and cyclins in regulating G1 to S progression and their synchronous dysregulation during tumor development required additional studies. Thus the state of the art shows that levels of p27 expression, and the role of p27 in the cell cycle are unpredictable in terms of diagnosing aggressiveness of cancer. The skilled artisan would have to perform an analysis that determined directly the correlation between p27 expression and aggressiveness of prostate cancer to practice the invention as claimed. As the results of such an analysis are clearly unpredictable given the lack of guidance in the specification, and the teachings of unpredictability in both the specification and the art, such experimentation is considered undue.

With regard to claims 2 and 3, the specification teaches that abundant amounts of p27 protein were detected in the ductal and acinar cells, as well as stroma cells and epithelial cells while 12 cases for benign prostate hyperplasia (BPH) showed low to undetectable levels of p27 (p. 26). Claims 2-3, however, are drawn to detecting a decrease in p27 protein or mRNA expression in an "appropriate sample of hyperplasia". Firstly, the specification does not define

what an "appropriate sample of hyperplasia" is. It is unclear from the teachings in the specification whether an 'appropriate sample' refers to a sample of hyperplasia from any tissue, or whether the term refers to a specific type of tissue. If the latter is the case, the specification does not teach what samples of prostate are "appropriate" for the skilled artisan to determine that a "decrease" in p27 expression is indicative of BPH. Secondly, the specification does not provide a basis for comparison for the skilled artisan to be able to determine what constitutes a "decrease" in p27 expression. The specification only teaches "abundant" expression in normal cells and "low" to undetectable levels in BPH cells and does not teach whether such results were statistically significant. As the specification does not teach the skilled artisan what constitutes a "decrease" in p27 expression such that BPH could be diagnosed based *solely* on such comparison, and no correlation is given in the art between amount of p27 expression and diagnosis of BPH, the skilled artisan would have to perform an analysis to quantitate levels of p27 expression in normal vs. BPH samples from all different types of tissue, the results of which are unpredictable and thus constitutes undue experimentation.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 2-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite in the recitation of "appropriate sample of the hyperplasia" as the claims do not make clear and the specification does not define what is considered an "appropriate sample" of a hyperplasia.

Applicant Note: it appears that the word benign has been misspelled in claim 2 as "beign".

5. No claims are allowable.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Thursday from 7:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa B. Arthur

LISA B. ARTHUR
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Jehanne Souaya

Jehanne Souaya
Patent examiner
July 2, 2001